

Group	Strain	Protein(s) Affected	Description	Reference
Parental	14028s	N/A	Wild-type parental strain; highly virulent, highly inflammatory	N/A
Metabolic Attenuation	$\Delta aroA$	3-phosphoshikimate 1-carboxyvinyltransferase	Mutant lacks enzyme connecting glycolysis to aromatic amino acid synthesis; expression of a variety of genes is affected	(1)
Defect in LPS Core	$\Delta galE$	UDP-galactose-4-epimerase	Mutant lacks the enzyme required to metabolize galactose, a core sugar in LPS	(2, 3)
	$\Delta rfaG$	Glucosyltransferase I	Mutant has highly truncated LPS; no outer core can be added to the inner core; there is no O-antigen	(1, 4)
	$\Delta rfaH$	Transcriptional antiterminator	Mutant has defective core LPS and lacks the O-antigen	(5)
Structural Change to Lipid A	$\Delta pagP$	Palmitoyl transferase for lipid A	Adds a palmitate to lipid A in response to membrane damage; lack of gene results in more hexa-acylated LPS (more immunogenic)	(6–9)
	$\Delta msbB$	(KDO)2-(lauroyl)-lipid IVA acyltransferase	Transfers myristate to lipid A; thought to be a significant factor in attenuation of tumor-targeting VNP20009	(10, 11)
	$\Delta lpxO$	dioxygenase for lipid synthesis	Adds a hydroxyl group to myristate at 3'; altered structure may have implications for TLR4 activation	(9)
	VNP20009	PurI, MsbB	PurI mediates purine biosynthesis; MsbB adds terminal myristate to lipid A. Administered to humans safely in two Phase I clinical trials	(10, 12)
	VNP20009 <i>msbB</i> ⁺	(KDO)2-(lauroyl)-lipid IVA acyltransferase	Used to elucidate the role of other mutations in VNP20009	(13)
Defect in O-antigen	Δrfc	O-antigen polymerase	O-antigen is not synthesized to its full length	(5)
	$\Delta rfbK$	phosphomannomutase	Mutant has no O-antigen	(14)
	$\Delta rfbP$	O-antigen transferase	Mutant has no O-antigen	(15)
	$\Delta manA$	mannose-6-phosphate isomerase	Mutant is unable to synthesize the O-antigen, but still expresses the full core lipid A	(2)
	$\Delta rfaL$	O-antigen ligase	Mutant has a complete LPS core but lacks the O-antigen	(4)
Other Mutations	$\Delta manC$	mannose-1-phosphate guanylyltransferase	Mutant produces less LPS, has improved ability to form biofilms, and induces lower reactive oxygen species (ROS) response in macrophages	(16)
	$\Delta csgA$	cryptic curlin major subunit	CsgA was shown to be a TLR2 PAMP; mutants have reduced production of fimbria	(17, 18)

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